Results are shown in the table.

Overall there were correlations between peak VO2 and strength ($r = 0.46$, $p < 0.0001$), quads CSA ($r = 0.355$, $p = 0.0002$) and 20 minute fatigue ($r = 0.4$ $p < 0.001$) and between the VE/VCO2 slope and strength ($r = 0.345$, $p < 0.0001$) quads CSA ($r = 0.28$, $p = 0.005$) and 20 minute fatigue ($r = 0.25$, $p = 0.008$). *Conclusions:* CHF patients are weak because of atrophy and reduced strength per unit muscle. The associations between oxygen consumption, the ventilatory response to exercise and muscle indices suggest that muscle abnormalities modify exercise capacity in CHF.

2:15

752-2 Relation Between Low-Intensity Exercise Capacity and Quality of Life in Patients With Mild to Moderate Congestive Heart Failure

D. Weilenmann, H.P. Brunner-La Rocca, B. Lüll, M. Schlumpf, W. Kiowski, F. Follath. *Division of Cardiology, Department of Medicine, University Hospital, Zurich, Switzerland*

Exercise capacity (EC) is an accepted prognostic factor in patients (P) with congestive heart failure (CHF). However, its relation to measures of quality of life (QOL) such as the "Minnesota living with heart failure questionnaire" (MQ) is poorly defined. Therefore, we repeatedly assessed the MQ and low-intensity and maximal EC during treatment with different doses of enalapril in 24 P (age: 52 ± 11 years) with impaired systolic left ventricular function (EF = 26 ± 6%) and mild to moderate CHF (NYHA: 2.1 ± 0.4). EC was assessed by a standard protocol treadmill ergospirometry (6 min low-intensity exercise followed by a maximal exercise ramp protocol; peak oxygen uptake (pVO_2), O_2-kinetics, total exercise duration (TED)).

No correlation was found between the total MQ score (SMQ) and pVO_2 ($r = -0.11$, ns). A moderate correlation existed between SMQ and TED ($r = -0.23$, $p < 0.05$), whereas SMQ and the O_2-deficit ($r = 0.43$, $p < 0.001$) as well as the mean response time (MRT [$t_{1/2}$ of increase in O_2-uptake]; $r = 0.46$, $p < 0.001$) were more tightly linked during low-intensity exercise. NYHA class correlated with all parameters (best with SMQ: $r = 0.45$, $p < 0.001$ and lowest with pVO_2: $r = -0.33$, $p < 0.005$).

Conclusion: P do not seem to notice the extent of impairment in pVO_2 during daily life. In contrast, the O_2-deficit correlated better with the SMQ indicating that increases of low-intensity exercise performance are perceived as better QOL. Our data, therefore, support the concept of using a submaximal stress test to evaluate the extent of impairment during daily life, and, accordingly, measures of QOL in P with CHF.

2:30

752-3 Clinical Relevance of Arterial Oxygen Saturation Instability to Detect Breathing Disorders in Chronic Heart Failure

A. Mortara, G.D. Pinna, R. Maestri, A. Prpa, F. Cobelli, P. Sleight [1], L. Tavazzi. *Division of Cardiology, "S. Maugeri" Foundation, IRCCS, Montescano, Pavia, Italy,* [1] *John Radcliffe Hospital, Oxford, UK*

Recently it has been shown that in chronic heart failure (CHF), Cheyne-Stokes (CS) respiration and periodic breathing (PB) are present during both day- and night-time. This altered ventilation is associated with marked oscillations of arterial oxygen saturation (SaO2). To address the relation between breathing disorders and modulation of SaO2 during awake day-time, 80 pts with mild to moderate CHF (age 51 ± 6 yrs, LVEF 27 ± 8%, NYHA cl. I–III, stable oral therapy) underwent simultaneous 20' recordings of instantaneous lung volume (ILV), beat-to-beat SaO2 (ear probe) and heart rate at baseline and during controlled breathing (12 breaths/min). Analysis of ILV revealed a normal respiratory pattern in 29 pts, while 51 had a persistent alteration of breathing, with a typical CS in 21 and a PB in 30. Overall variability of SaO2 was obtained by analysis of the standard deviation (SD) of the beat-to beat signals. SaO2 was significantly reduced in CS and PB (respectively, 93.0 ± 1.8 and 93.8 ± 2% vs 94.2 ± 1.6%, both $p < 0.02$) and SD of SaO2 was higher (1.5 ± 0.6 and 0.7 ± 0.2% vs 0.4 ± 0.1%, $p < 0.01$ and $p < 0.03$) as compared to normals. Controlled ventilation eliminated CS and PB in all patients with a significant increase in SaO2 (CS = +2.5%, $p < 0.001$, PB = +1.4%, $p < 0.01$); SaO2 variability remained unchanged in normals, while it was markedly reduced in CS and PB (CS = 0.4 ± 0.2%, PB = 0.3 ± 0.2%, $p < 0.02$ vs baseline). By R.O.C. it was found that SD of SaO2 ≥1% had a sensitivity of 86% and a specificity of 100% in identifying CHF patients with CS. Thus, in CHF, abnormalities of breathing activity cause a marked instability of SaO2 predisposing to prolonged periods of hypoxia. It is suggested that continuous beat-to-beat analysis of SaO2 and the simple calculation of SD of the mean may be a reliable marker for breathing disorders both during day and night recordings.

2:45

752-4 Similar Efficacy (but Different Mechanisms) on Exercise Capacity of Losartan (LOS) and Enalapril (EN) in Chronic Heart Failure (CHF)

M. Guazzi, P.G. Agostoni, G.C. Marenzi, G. Melzi, M.D. Guazzi. *University of Milan, C.N.R., Milan, Italy*

Amelioration of respiratory function and exercise capacity with ACE-inhibition in CHF is antagonized by aspirin (AS), suggesting a bradykinin-prostaglandin mediated effect. A comparative study with EN vs the AT1 blocker, LOS, alone and in combination with AS, may help to define efficacy of one drug as compared to the other, selectivity of AS counteraction, role of bradykinin-prostaglandin activation. 16 patients with CHF (NYHA class III), treated with digoxin and furosemide, received (double-blind, random order), placebo (PL), EN (20 mg), AS (325 mg), LOS (50 mg), EN+AS, LOS+AS for 15 days each. Lung diffusion capacity (DLCO, mmHg/min/kg), exercise tolerance time (TT, sec), vital capacity (VC, l) as well as oxygen uptake (VO2 p), dead space/tidal volume ratio (VD/V p) at peak exercise were tested at the end of each step.

	VO2 p	TT	VD/VTp	VC	DLCO
PL	15.7 ± 3	572 ± 181	0.21 ± 0.03	3.0 ± 0.9	19 ± 3
EN	18 ± 4#§	631 ± 154#§	0.20 ± 0.03	3.3 ± 0.6	22 ± 4#§
EN+AS	16 ± 4	590 ± 130	0.22 ± 0.05	3.1 ± 0.6	19 ± 4
AS	15 ± 5	579 ± 133	0.19 ± 0.05	3.0 ± 0.9	18 ± 6
LOS	18 ± 4#§	650 ± 146#§	0.19 ± 0.03#§	3.0 ± 1.0	20 ± 3
LOS+AS	17 ± 6#§	659 ± 133#§	0.19 ± 0.03#§	3.1 ± 1.0	20 ± 3

#$p < 0.05$ vs. PL; § = $p < 0.05$ vs. EN+AS. Mean values (± 1 SD).

Conclusions: Effectiveness of the two drugs on exercise capacity (TT and VO2 p) is similar but probably mediated through different mechanisms, as suggested by a selective counteraction of AS against EN. Prostglandin activation occurs with the ACE-inhibitor and not with the AT1 blocker and importantly participates in raising lung diffusion and functional capacity. Improvement in TT and VO2 p with LOS is dissociated from significant influences on the respiratory function.

3:00

752-5 Effects of Losartan on Exercise Capacity, Morbidity and Mortality in Patients with Symptomatic Heart Failure

G. Klinger, N. Jaramillo, H. Ikram, M. Higginbotham, R. Lang, D. Kraus, L. Washington, D. Sharma, W. Grossman. *Merck & Co., Inc., West Point, PA, USA*

Losartan (L) is a specific angiotensin II (AngII) type 1 receptor antagonist which blocks the effects of AngII generated from both ACE and non-ACE dependent pathways. Thus, L may block the effects of AngII more completely than an ACE inhibitor. Two multicenter, double-blind, placebo-controlled, exercise studies were performed to assess the efficacy and safety of L in patients with heart failure (HF). Patients with NYHA Class II–IV HF and ejection fraction ≤40% were randomized in a 2:1 ratio (L:placebo [P]). Changes in maximal exercise time (ET-primary endpoint) after 12 weeks of treatment were not different between groups. Median increases (sec) were 55 and 45 for L and P, respectively, in the U.S. study and 90 and 100 for L and P in the International study. However, each study showed fewer deaths and hospitalizations for HF during treatment with L (Table). A pre-specified meta-analysis combining the 2 studies showed a significant reduction in death and hospitalization for HF during treatment with L.

	U.S. (n = 351)		Int'l (n = 385)		Combined	
	L	P	L	P	L	P
Death	1.7%	3.5%	1.2%*	6.9%	1.4%*	5.3%
HF hospitalization	4.2%	8.8%	2.0%	5.3%	3.1%*	6.9%

* $p < 0.05$ vs. pbo

Conclusion: Compared to placebo, treatment with losartan for 12 weeks did not improve ET but significantly reduced morbidity and mortality in patients with heart failure.